

## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or owner's file reference 520-204-WO	<b>FOR FURTHER ACTION</b>		See Form PCT/ISA/220 as well as, where applicable, item 6 below
International application No. PCT/EP2005/050805	International filing date (day/month/year) 25/02/2005	(Earliest) Priority Date (day/month/year) 25/02/2004	
Applicant  ZOENE A/S			
<p>This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.</p> <p>This International Search Report consists of a total of <u>      </u> sheets.</p> <p><input checked="" type="checkbox"/> It is also accompanied by a copy of each prior art document cited in this report.</p>			
<p>1. Basis of the report</p> <p>a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).</p> <p>b. <input type="checkbox"/> With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.</p> <p>2. <input checked="" type="checkbox"/> Certain claims were found unsearchable (See Box II).</p> <p>3. <input type="checkbox"/> Unity of invention is lacking (see Box III).</p> <p>4. With regard to the title,</p> <p><input checked="" type="checkbox"/> the text is approved as submitted by the applicant.</p> <p><input type="checkbox"/> the text has been established by this Authority to read as follows</p>			
<p>5. With regard to the abstract,</p> <p><input checked="" type="checkbox"/> the text is approved as submitted by the applicant.</p> <p><input type="checkbox"/> the text has been established, according to Rule 36.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.</p>			
<p>6. With regard to the drawings,</p> <p>a. The figure of the drawings to be published with the abstract is Figure No. <u>      </u>.</p> <p><input checked="" type="checkbox"/> as suggested by the applicant.</p> <p><input type="checkbox"/> as selected by this Authority, because the applicant failed to suggest a figure.</p> <p><input type="checkbox"/> as selected by this Authority, because this figure better characterizes the invention.</p> <p>b. <input type="checkbox"/> none of the figures is to be published with the abstract.</p>			

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/050805

**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. A61K31/192 A61K31/7052 A61K38/45 A61K45/06 A61P35/00

According to International Patent Classification for Chemical Patent Classification and EPO

**B. FIELDS SEARCHED**

Minimum documentation - or broad publication systems (indicated by circled symbols):  
 A61K A61P

Documentation sources of other broad publication systems relevant to the subject matter specified in the table are indicated in the table under **C**

For input data base, consult **D** (see the International search report of data base and relevant search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Character of document with indication, where appropriate, of the relevant passage(s)	Relevant to claim No.
Y	<p>ASKLUND THOMAS ET AL: "Gap junction-mediated bystander effect in primary cultures of human malignant gliomas with recombinant expression of the HSVtk gene."  EXPERIMENTAL CELL RESEARCH, vol. 284, no. 2, 1 April 2003 (2003-04-01), pages 185-195, XP002377912 ISSN: 0014-4827 page 191-194, paragraph entitled "Discussion"; figure 6</p> <p>----- -/-</p>	1-6, 11-68

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*T\* document which may throw doubt on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*C\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents such combination being obvious to a person skilled in the art

\*S\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

24 April 2006

17/05/2006

Name and mailing address of the ISA

Authorized officer

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Form PCT/ISA/2005 (second sheet) (January 2004)

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International Application No

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C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Characteristics of the document and its approximate date of the relevant event	Relevant to claim No
Y	ALMQVIST P M ET AL: "DIFFERENTIATION OF HUMAN PRIMARY GLIOBLASTOMA CELLS BY 4 - PHENYLBUTYRATE." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2002, 2002, pages Abstract No. 802.8 URL- <a href="http://sf.">http://sf.</a> XP009065441 & 32ND ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE: ORLANDO, FLORIDA, USA; NOVEMBER 02-07, 2002 abstract	1-6, 12-68
Y	ALTERNBURG B C ET AL: "MODIFICATION OF THE PHENOTYPE OF MURINE SARCOMA VIRUS TRANSFORMED CELLS BY SODIUM BUTYRATE EFFECTS OF MORPHOLOGY AND CYTOSKELETAL ELEMENTS" EXPERIMENTAL CELL RESEARCH; vol. 102, no. 2. 1976, pages 223-231, XP009065490 ISSN: 0014-4827 page 228-231. paragraph entitled "Discussion"	1-5, 11-56, 58,59, 61-68
X	JIAN WEIGUO ET AL: "Combination of adenovirus mediated suicide gene therapy with the histone deacetylase inhibitors butyrate, phenylbutyrate and electroporation in bladder cancer in vitro and in vivo." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 44, July 2003 (2003-07), pages 1300-1301, XP001247005 & 94TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; WASHINGTON, DC, USA; JULY 11-14, 2003 ISSN: 0197-016X abstract	1-6, 11-68
X	CHUNG Y L ET AL: "A novel approach for nasopharyngeal carcinoma treatment uses phenylbutyrate as a protein kinase C modulator: implications for radiosensitization and EBV-targeted therapy." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. APR 2000, vol. 6, no. 4, April 2000 (2000-04), pages 1452-1458, XP002377913 ISSN: 1078-0432 page 1456-1457. paragraph entitled "Discussion"	1-6, 11-68

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International Application No

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## (Continued) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Characteristics of publication, which appear to be relevant	Page, line to claim No.
X	KWON H ET AL: "HERPES SIMPLEX VIRUS THYMIDINE KINASE GENE THERAPY DELIVERED BY RETROVIRAL OR ADENOVIRAL VECTOR IN MOUSE MODEL OF LEWIS LUNG CARCINOMA" TUBERCULOSIS AND RESPIRATORY DISEASES, SN. KR, vol. 49, no. 3, September 2000 (2000-09), pages 298-309, XP001208119 ISSN: 0378-0066 abstract on pages 298-299	1-6, 11-68 6
X	CAMACHO L H ET AL: "Transcription modulation: A pilot study of sodium phenylbutyrate plus 5-azacytidine" BLOOD, vol. 98, no. 11 Part 1, 16 November 2001 (2001-11-16), page 460a, XP009065447 & 43RD ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY, PART 1: ORLANDO, FLORIDA, USA; DECEMBER 07-11, 2001 ISSN: 0006-4971 abstract	1-6, 11, 31, 32, 34, 45-47, 53-58, 60-62, 64-68 7
X	HUANG Y ET AL: "Enhanced growth inhibition and differentiation of fluorodeoxyuridine-treated human colon carcinoma cells by phenylbutyrate." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, OCT 1998, vol. 4, no. 10, October 1998 (1998-10), pages 2503-2509, XP002377914 ISSN: 1078-0432 page 2508, paragraph entitled "Discussion"	1-6, 11, 31, 32, 34, 45-47, 53-58, 60-62, 64-68 8
P, X	AMMERPOHL O ET AL: "HDAC1 phenylbutyrate increases bystander killing of HSV-tk transfected glioma cells" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 324, no. 1, 5 November 2004 (2004-11-05), pages 8-14, XP004605891 ISSN: 0006-291X page 12-13, paragraph entitled "Discussion"	1-68 9

-/-

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Character of document with indication where appropriate of the relevant passage	Referred to in the report
P, X	ROBE PIERRE A ET AL: "Modulation of the HSV-TK/ganciclovir bystander effect by n-butyrate in glioblastoma: Correlation with gap-junction intercellular communication" INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 25, no. 1, July 2004 (2004-07), pages 187-192, XP009065479 ISSN: 1019-6439 189-191, paragraph entitled "Discussion" -----	1-5, 11-56, 58,59, 61-68
P, Y	ASKLUND T ET AL: "Histone deacetylase inhibitor 4-phenylbutyrate modulates glial fibrillary acidic protein and connexin 43 expression, and enhances gap-junction communication, in human glioblastoma cells" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 40, no. 7, May 2004 (2004-05), pages 1073-1081, XP004502680 ISSN: 0959-8049 page 1077-1080, paragraph entitled "Discussion" -----	1-6, 12-68

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2005/050805

### Box II Observations where certain claims were found unsearchable (Continuation of item 3 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Rule 39.1(iv) PCT:** Although claims 32-46, 58-61 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out specifically.
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.